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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/627,314	07/25/2003	Elisabeth Henriette Burger	116.003	1901

7590 09/28/2006

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EXAMINER	
CORDERO GARCIA, MARCELA M	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 09/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/627,314	BURGER, ELISABETH HENRIETTE	
	Examiner	Art Unit	
	Marcela M. Cordero Garcia	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18 and 21-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18 and 21-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of LLLFLLKKRKKRKY (a.k.a. DHVAR-5) and TGFβ in the replies filed on December 7, 2005 and July 12, 2006 is acknowledged. Based on the amendments and arguments presented the traversal is found persuasive, therefore the restriction requirement mailed on October 7, 2005 is therefore vacated. Claims 1-18 and 21-23, drawn to a resorbable bone substitute are presented for examination on the merits.

Claim Objections

Claim 23 is objected to because of the following informalities: at line 4, the word "submcomponent" appears to contain a typo. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is rendered vague and indefinite because it is unclear, as in line 6 it refers to "claims 709" which do not exist.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-13, 15-18 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burger et al. (WO 00/01427) in view of Constantino et al. (WO 96/39202) [citation B in the IDS of 07/03].

Burger et al. teach a resorbable bone substitute for in vivo implantation, comprising bone cement material, an antimicrobial agent (LLLFLLKKRKKRKY) (e.g., claim 23) and albumin as a protein carrier protein to hold the antimicrobial peptide(s) in solution (page 6, lines 26-32). Please note that the antimicrobial agent LLLFLLKKRKKRKY would inherently have a fast release profile.

Burger et al. does not teach a bone substitute with TGFβ, nor does it teach mixing solutions containing TGFβ and albumin and antimicrobial peptide.

Constantino et al. teach a resorbable bone substitute for in vivo implantation, comprising bone cement material, an antimicrobial (antibiotic) agent, and bone growth factors such as TGFβ and albumin (e.g., pages 17-18, page 31, last line, pages 32, page 33, lines 1-21), and forming a liquid phase with a protein carrier protein such as albumin and bone growth factors (see, e.g., page 32, lines 24-28, page 33, lines 1-28 and page 34, lines 1-4, page 35, lines 3-28, page 36, lines 1-12, page 37, lines 1-12).

The bone growth factor may be from about 10-50 μg to about 100-500 μg for cm^3 of the formulation (e.g., page 35, lines 17-21, page 37, lines 8-12). Please note that TGFβ having a slow release profile would be inherent to the instantly claimed composition.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the resorbable bone substitute of Burger et al. by adding a bone growth factor (TGFβ) as taught by Constantino et al. and/or to make the composition by mixing the bone growth factor with albumin in a liquid medium and adding the antimicrobial peptide in a liquid medium as well. The skilled artisan would have been motivated to do so because Constantino et al. teach mixing albumin with bone growth factors such as TGFβ in a liquid medium and because Burger et al. teach dissolving the antimicrobial peptide in a liquid medium (e.g., page 7, lines 3-15).

There would have been a reasonable expectation of success, given that bone growth factors such as TGFβ were known to cause induction of new bone formation upon in vivo implantation as taught by Constantino et al. (e.g., page 35, lines 3-21). The adjustment of particular conventional working conditions [e.g., selecting other antimicrobial peptides of similar conformation and a length of 10-25 aminoacids (e.g., claim 1 of WO 00/01427), determining concentrations of the active ingredients, volume ratios of the mixing solutions and/or making kits thereof within such resorbable bone compositions (e.g., Constantino et al., page 35, lines 17-21, page 37, lines 8-12, claims 102, 115-118, 120-121)] is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a

whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-5, 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang (US 6,485,751) in view of Van Nieuw Amerongen et al. (WO 01/56627).

Wang teaches a resorbable bone substitute for in vivo implantation, comprising bone cement material, an antimicrobial (antibiotic) agent and a bone growth factor such as TGFβ (e.g., Fig. 1, column 1, lines 60-67, column 2, lines 5-37; column 4, lines 65-67 and column 5, lines 1-4). Please note that TGFβ having a slow release profile would be inherent to the instantly claimed composition.

Wang does not teach the antimicrobial agent being LLLFLLKKRKKRKY (SEQ ID NO. 4) or an antimicrobial agent with fast release profile.

Van Nieuw Amerongen et al. (WO 01/56627) teach the antimicrobial agent LLLFLLKKRKKRKY (e.g., claim 5, Tables 1-2) for coating implants composed, e.g., of apatites or cement in order to prevent/inhibit tissue loss and bone degradation around the implants (e.g., page 9-19). Please note that having a slow release profile would be inherent to such peptide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the apatite cement composition of Wang by utilizing the antimicrobial agent LLLFLLKKRKKRKY as taught by Van Nieuw Aromgen et al. The skilled artisan would have been motivated to do so because Wang teaches bone cement materials with antibiotics for curing infection (column 4, lines 65-67, column 5,

line 1) and because newly discovered peptide could be used for infections resistant against most common antibiotics and because Van Nieuw Aromgen et al. teach that implants (including those made of cement and/or apatites, e.g., page 1, lines 18) may cause infections that are highly resistant against usual antimicrobial agents (page 2, lines 8-27). There would have been a reasonable expectation of success, given that LLLFLLKKRKKRKY was known to have a broad spectrum of action as taught by Van Nieuw Aromgen et al. (see Tables 1-2 for DHVAR-5). The adjustment of particular conventional working conditions [e.g., selecting other antimicrobial peptides of similar conformation and a length of 10-25 aminoacids (e.g., claim 8 of WO 01/56627), determining the amount of bone growth factor/antimicrobial peptide added within such bone substitute composition] is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan. Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

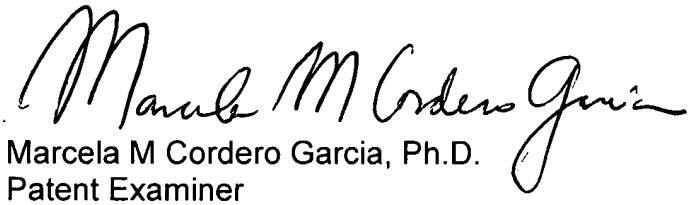
No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

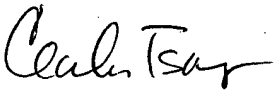
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Marcela M Cordero Garcia, Ph.D.
Patent Examiner
Art Unit 1654

MMCG 09/06



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